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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/652,799	08/29/2003	Barry Eisenstein	50150/005003	2013

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EXAMINER	
FUBARA, BLESSING M	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 04/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/652,799	EISENSTEIN, BARRY	
	Examiner	Art Unit	
	Blessing M. Fubara	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *01/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of request for extension of time, request for reconsideration and remarks, all filed 10/21/04. Examiner further acknowledges the receipt of IDS filed 01/13/05. Claims 1-75 are pending.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating a subject having an infection of clostridium difficile or inhibiting infection of clostridium in a subject, does not reasonably provide enablement for preventing infection of clostridium difficile in a subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of protection sought by the claims is prevention/preventing infection of clostridium difficile and the scope of enablement provided to one skilled in the art by applicant's disclosure is determination of minimum inhibitory concentration of rifalazil concentration of clostridium difficile and treatment/treating clostridium difficile associated disease. Specifically, the treatment regimen in Example 1 monitors the survival, weight variations, identification of clostridium difficile toxins in cecal content and histological damage to the ceca after oral gavage of clostridium difficile and administration of rifalazil or rifalazil in combination with a second drug compound. An optimal dosage is then determined. The Anton work concludes treatment

and not prevention. Thus, the scope of enablement provided by applicant's disclosure is not commensurate with the protection sought by the claims. Secondly, one skilled in the art is not enabled by the to make and use the entire scope of the claimed prevention/preventing without undue experimentation since no guidance is provided on how the preventing of an infection of clostridium difficile in a subject is given. Guidance is only provided for a) how to determine optimum dosage of rifalazil or rifalazil in combination with a second drug compound, and b) how to determine the minimum inhibitory concentration of rifalazil for clostridium difficile. The standard for prevention/preventing is high and the high standards require that guidance be provided on how the infection of clostridium difficile is prevented. However, no guidance is provided and there is no experimental data showing prevention/preventing.

Claim Rejections - 35 USC § 101/Printed Matter Rejection

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 54-75 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 54 recites "instruction" as part of the claimed product/composition and a mere arrangement of printed matter, though seemingly a "manufacture," is as not within the statutory classes. See In re Miller, 418 F.2d 1392, 164 USPQ 46 (CCPA 1969); Ex parte Gwinn, 112 USPQ 439 (Bd. App. 1955); and In re Jones, 373 F.2d 1007, 153 USPQ 77 (CCPA 1967).

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (i) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-11, 13-18, 20-27, 29-45, 48-50, 54-65, 67-73 are rejected under 35 U.S.C. 102(e) as being anticipated by Michaelis et al. (US 2004/0034021).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Michaelis discloses method of treating infection of clostridium difficile by administering composition that comprises rifalazil; the composition that is administered may further contain one or more antibiotics (paragraphs [0013], [0014], [0054], [0114], [0115], [0124], [0145], and claims 1-62).

Claim Rejections - 35 USC § 103

6. Claims 1-11 and 54-58 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chamberland et al. (US 6,114,310) in combination with Rose et al. (US 6,316,433).

Applicant argues that Chamberland does state that rifamycins can be or should be used to treat *C. difficile* but rather that Chamberland discloses 89 different bacteria that can be inhibited by the use of an efflux pump inhibitor. Applicant further argues Chamberland does not focus on rifamycins as therapeutic agents but the focus of Chamberland is on efflux pump inhibitors, and further that Chamberland lists rifamycins as one of nine different classes of "possible" antibacterial agent and one of 141 "possible" antibacterial agents. Furthermore, applicant argues that Chamberland cannot specifically teach rifamycin for treating clostridium difficile because "inclusion of *C. difficile* and rifamycin in two such all-inclusive lists cannot form the basis for the assertion that Chamberland specifically teaches." Applicant then states that Rose, the secondary reference does not remedy the deficiency of Chamberland even if Rose discloses using rifalazil to treat bacterial infection by a once-weekly administration of the rifalazil.

7. Applicant's arguments filed 10/21/04 have been fully considered but they are not persuasive.

While Examiner agrees with applicant that Chamberland discloses efflux pump inhibitors for treating microbial infections, it is respectfully noted that Chamberland (column 16, lines 22-31) uses antimicrobial agent and efflux pump inhibitor. Although Chamberland's focus may not be specifically rifamycin, Chamberland does list rifamycin for use with the efflux pump inhibitor and the list is not exhaustive. Rose is relied upon for a teaching that rifalazil is a known

rifamycin and thus contributes to the disclosure of Chamberland that rifamycin, (and example of which is rifalazil according to Rose) is used in combination with efflux pump inhibitors to treat microbial infections. It is also respectfully noted that the claims do not exclude efflux pump inhibitors.

8. Claims 13, 34, 35, 37-53, 59 and 73-75 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chamberland et al. (US 6,114,310) in combination with Rose et al. (US 6,316,433) in further combination with Bostwick et al. (US 5,773,000).

Applicant argues that Chamberland does not teach that rifamycin can be used to treat *C. difficile* infections and does not guide the skilled artisan to select rifamycin for the treatment of infection of *C. difficile* and that Rose does not remedy the deficiency. Applicants further argue that Bostwick does not remedy the deficiency because Bostwick does not disclose rifalazil for the treatment of *C. difficile* infection. Applicant argues that Bostwick requires the use of antibodies for *C. difficile* infection and discusses advantages for using antibodies over antibacterial agents. Therefore, applicant argues that Bostwick teaches away from the claimed invention since the skilled artisan, from reading Bostwick, would be motivated to combine two antibodies.

9. Applicant's arguments filed 10/21/04 have been fully considered but they are not persuasive.

Chamberland (column 16, lines 22-31) uses antimicrobial agent and efflux pump inhibitor. Rose is relied upon for a teaching that rifalazil is a known rifamycin and thus contributes to the disclosure of Chamberland that rifamycin, (and example of which is rifalazil according to Rose) is used in combination with efflux pump inhibitors to treat microbial

infections. Bostwick (abstract; column 2, line 63 to column 3, line 11) discloses treating clostridium difficile associated diseases with antibodies and with antibodies in combination with antibiotics such as vancomycin bacitracin and metronidazole. Thus Bostwick discloses using combination of antibodies and antibiotics to treat *C. difficile* and does not teach away form the claimed invention. It is also respectfully noted that Bostwick discloses: "because the present antibodies first eliminate the *C. difficile* toxins, **it is also advantageous to administer to patients suffering from C. difficile associated diseases a *combination of the antibodies of the present invention with antibiotics prior known for treating pseudomembranous colitis and/or antibiotic associated diarrhea.* Such antibiotics are for example vancomycin, bacitracin and metronidazole**. Because of the **speedy and quick elimination of the *C. difficile* toxins, the combination of antibody and antibiotic may be synergistic requiring much less antibiotic normally used in treating such diseases with results of decreased symptoms development, faster symptomatic relief and lower relapse rate.** Recognized doses for administering metronidazole for example is 250 mg four times a day, and oral vancomycin is 125 mg four times a day. Administration of these antibiotics with the antibody of the present invention would result in use of substantially reduced dosage of antibiotics.

10. Claims 12, 14-33, 36 and 60-72 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chamberland et al. (US 6,114,310) in combination with Rose et al. (US 6,316,433) in further combination with the admission of applicant in the specification.

Applicant argues that the combination of antibiotics and rifalazil was not known at the time the invention was made because rifalazil was not taught or disclosed by Chamberland or Rose or elsewhere in the prior art for use in treating *C. difficile.*

Applicant further argues that, "the fact that other antibiotics were known and their dosages determined is of no significance to the patentability of Applicant's basic invention – the use of rifalazil to treat *C. difficile*."

11. Applicant's arguments filed 10/21/04 have been fully considered but they are not persuasive.

Chamberland discloses treating *C. difficile* infection with a combination of efflux pump inhibitors and antibiotics and rifamycin is one of the general classes of antibiotics disclosed (see also claims 1, 5, 10 and 15). Rose discloses that rifalazil belongs to the general class of rifamycin and rifalazil is used to treat bacterial infections. Thus it would be obvious that a member of the rifamycin class/group of antibiotics would be used to treat *C. difficile*, specifically, in this case, rifalazil, a rifamycin can be used to treat *C. difficile* infection.

12. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara
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